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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WRIGHT, SONYA N	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,884	BEATCH ET AL.	
	Examiner	Art Unit	
	Sonya Wright	1626	

-- The MAILING DATE of this communication appears on the cover she t with the correspondenc addr ss --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-71,74-83 and 86-89* is/are rejected.

7)☒ Claim(s) *84 and 85* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1103* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-89 are pending in this application.

Election/Restrictions

Applicant's election with traverse of Group II in the response filed July 25, 2003 is acknowledged. The traversal is on the ground(s) that Applicants believe that examination of the entire genus of claim 1 is appropriate and does not cause an undue burden on the Examiner. This is not found persuasive because the claims herein lack unity of invention under PCT Rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art. The claims are drawn to a compound of formula (I) with variables n, X, Y, R1, R2, R3, R4, R5, etc. . . which do not define a contribution over the prior art. The variables are broadly defined and when taken as a whole result in vastly different compounds. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Additionally, the vastness of the claimed subject matter and the complications in understanding the claimed subject matter imposes a burden on any examination of the claimed subject matter.

The following generic embodiment is identified for examination along with the elected group: Compounds according to claim 1 wherein R1 and R2 are taken together to form a morpholine ring which may be substituted as defined; A is a C3-C13carbocyclic ring and ring systems selected from formulae (III), (IV), (V), (VI), (VII) and (VIII); and all other variables are as defined. The remaining subject matter of

claims 1-89 is withdrawn from further consideration under 37 CFR 1.142(b) as constituting other patentably distinct inventions. The withdrawn compounds contain varying functional groups such as the varying heterocycles encompassed by the ring of formula (II). The varying heterocycles encompassed by the ring of formula II are variously classified. Therefore, the subject matter which is withdrawn from consideration as being non-elected subject matter differs materially in structure and composition and has been restricted properly. A reference which anticipated the elected subject matter would not render obvious the withdrawn subject matter and fields of search are not co-extensive.

Claim Objections

Claims 1-89 are objected to because of the following informalities: Claims 1-89 contain non-elected subject matter. It is suggested that Applicant limit the claims to the embodiment identified for examination (supra). Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 4 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-71 and 74-89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

1) Nature of invention.

2) State of prior art.

3) Level of ordinary skill in the art.

4) Level of predictability in the art

5) Amount of direction and guidance provided by the inventor.

6) Existence of working examples.

7)Breadth of claims.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

1) Nature of the invention.

Claims 5, 8-71, 74-83, and 86-89 are directed to preventing arrhythmia, diseases of the central nervous system, convulsions, epileptic spasms, depression, anxiety, schizophrenia, Parkinson's disease, respiratory disorders, cycstic fibrosis, asthma, cough, inflammation, arthritis, allergies, gastrointestinal disorders, urinary incontinence, irritable bowel syndrom, cardiovascular diseases, cerebral or myocardial ischemias, hypertension, long-QT syndrome, stroke, migraine, ophthalmic diseases, diabetes, myopathies, Becker's myotonia, myasthenia gravis, paramyotonia congentia, malignant hyperthemia, hyperkalemic periodic paralysis, Thomsen's myotonia, autoimmune disorders, graft rejection in organ transplantation or bone marrow transplantation, heart failure, hypotension, Alzheimer's disease, dementia, alopecia, artial arrhythmia, ventricular arrhythmia, atrial fibrillation, and ventricular fibrillation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

2) State of the prior art.

On page 1 of the specification, Applicant states that that both atrial arrhythmias and ventricular arrhythmias are known. On page 1 of the specification, Applicant further states that Class I antiarrhythmic compounds have been used to treat supraventricular arrhythmias and ventricular arrhythmias. On page 2 of the specification, Applicant provides journal articles regarding subject matter such as the use of Class Ia, Ic, and III antiarrhytmic drugs to convert recent onset AF to sinus rhythm. However, the prior arts do not indicate that the instant compound is useful in the prevention of all forms of diseases as claimed in claims 5, 8-71, 74-83, and 86-89.

3) Level of ordinary skill in the art.

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the instant compound in the prevention of diseases as claimed in claims 5, 8-71, 74-83, and 86-89.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

4) Level of predictability in the art.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Hence, in the absence of a showing of the prevention of all diseases as claimed in claims 5, 8-71, 74-83, and 86-89, one of skill in the art is unable to fully predict possible results from the

administration of the compound of claim 1 due to the unpredictability of the art pertaining to the diseases of claims 5, 8-71, 74-83, and 86-89..

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

5) Amount of direction and guidance provided by the inventor.

Applicant provides limited guidance regarding the use of the instant compound in the prevention of the diseases in claims 5, 8-71, 74-83, and 86-89. On pages 23-29 Applicant provides information on compositions of the instant compound and modes of administration. On pages 29-34 Applicant provides information on pharmacological testing. The guidance is limited because various forms of the diseases of claims 5, 8-71, 74-83, and 86-89 have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol.

6) Existence of working examples.

Applicant provides limited working examples of how the instant compound is used on pages 38-51. Applicant provides Example 4, assessment of antiarrhythmic efficacy; Table 1; Table 2; Example 5, measurement of ECG parameters; Table 3; Example 6, assessment of sodium channel blockage; Table 4; Example 7, Canine vagal-AF model; an atrial fibrillation model; measurement of electrophysiological

variables and vagal response; experimental procols, including Table 5; also, Example 8, acanine sterile pericarditis model; and a drug efficacy testing protocol; etc. . . However, the limited examples do not provide sufficient evidence to support the claims drawn to the prevention of the diseases in claims 5, 8-71, 74-83, and 86-89.

7) Breadth of claims.

Claims 5, 8-71, 74-83, and 86-89 are extremely broad due to the large number of diseases encompassed by each claim. Applicant has not provided sufficient evidence to support claims drawn to preventing all forms of the diseases in claims 5, 8-71, 74-83, and 86-89.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

In view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test how the instant compound is useful in the prevention of all diseases in claims 5, 8-71, 74-83, and 86-89, with no assurance of success.

These rejections can be overcome by Applicant deleting the term "or preventing" or "or prevent" in claims 5, 8-71, 74-83, and 86-89.

Further, claims 6 and 7 are drawn to "a method for modulating ion channel activity in a warm-blooded animal". This is a broad method of use, and Applicant has

not provided support that the instant compound is useful in modulating ion channel activity in a warm-blooded animal in all instances. It is suggested that Applicant limit claims 6 and 7 each to a to specific disease related to ion channel activity, which is supported in the specification.

Claims 8 and 9 are drawn to the treatment or prevention of "diseases of the central nervous system". Claims 30 and 31 are drawn to the treatment or prevention of allergies". Claims 38 and 39 are drawn to the treatment or prevention of "cardiovascular diseases". Claims 68 and 69 are drawn to the treatment or prevention of "autoimmune disorders". The diseases listed in claims 8, 9, 30, 31, 38, 39, 68, and 69 are all broad terms. Each disease listed in claims 8, 9, 30, 31, 38, 39, 68, and 69 contains various forms which require different treatment protocol. Applicant does not support that the instant compound can treat or prevent all forms of the diseases in claims 8, 9, 30, 31, 38, 39, 68, and 69. In addition to deleting "or preventing" or "or prevent" in claims 8, 9, 30, 31, 38, 39, 68, and 69, it is suggested that Applicant limit claims 8, 9, 30, 31, 38, 39, 68, and 69 to specific disorders which are treatable by the instant compound. If claims 8, 9, 30, 31, 38, 39, 68, and 69 are limited to specific disorders, each specific disorder should be supported in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> *The specification shall conclude with one or more claims particularly pointing out and distinctly* claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 provides for the use of the instant compounds in medicaments, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Duplicate Claims

Applicant is advised that should claim 5 be found allowable, claims 86 and 87 will be objected to under 37 CFR 1.75 as being substantial duplicates thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The subject matter of claims 86 and 87 is encompassed in claim 5. Therefore, claims 86 and 87 are duplicates of claim 5.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.

Joseph K. McKane

Supervisory Patent Examiner

Group 1600

Sonya Wright

November 2, 2003